SIMULTANEOUS COMPARISONS OF MULTIPLE TREATMENTS TO TWO (OR MORE) CONTROLS

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ABSTRACT

Dunnett (1955) developed a procedure comparing m treatments to one control with an exact overall type I error of α when all sampling distributions are normal. Sometimes it is desirable to compare m treatments to $k \geq 2$ controls. In particular, it is often desired to compare m treatments with two controls. For instance, several new treatments (e.g., pain relievers) could be compared to two standard treatments (e.g., Aspirin and Tylenol). Alternatively, a standard treatment could be very expensive, difficult to apply and/or have bad side effects, making it useful to compare each new treatment to both standard treatment and no treatment (Placebo).

Dunnett's method is expanded here to give comparisons of mean values for m treatments to mean values for $k \geq 2$ controls at an exact overall type I error of α when all sampling distributions are normal. Tabled values needed to make exact simultaneous comparisons at $\alpha = .05$ are given for k=2. An application is made to an illustrative example from the literature.

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KEY WORDS: Simultaneous Inference; Multiple Treatments; Multiple Controls; Dunnett's Procedure.

I. INTRODUCTION

Simultaneous comparison of m new treatments to one control has been well studied. The standard situation modeled is for n observations, sampled from each treatment group and the control group with independence of all observations, each control group observation distributed $N(\mu_c, \sigma^2)$, and each observation from treatment group j distributed $N(\mu_{t_j}, \sigma^2)$ for $j=1,\ldots,m$. Confidence intervals for $(\mu_{t_j} - \mu_c)$, the difference between each treatment mean and the control mean, are desired (the treatment being declared different from the control if the interval doesn't cover zero). It is important to limit the

probability of one, or more, confidence intervals not containing the true values (overall type I error) to some value α (usually α=.05) to prevent spurious findings.

Often, the investigator is only interested in a lower bound estimate for the improvement each treatment gives over the control. When larger means are desirable, one sided lower confidence intervals of the form:

$$(\mu_{t_j} - \mu_c) \geq L_j \text{ (for } L_j \text{ some function of the data) } j=1,\ldots,m$$

can be used. If smaller means are desirable, then one sided upper confidence intervals can be used. From now on WLOG we assume larger means are desirable. Sometimes the investigator wishes to have both upper and lower bounds for the improvement each treatment gives over the control, requiring two sided confidence intervals of the form:

$$L_j \leq (\mu_{t_j} - \mu_c) \leq U_j \text{ (for } L_j \text{ and } U_j \text{ some functions of the data) and } j=1,\ldots,m.$$

Dunnet's (1955) well known procedure gives one sided (or two sided) confidence intervals with a simultaneous overall type I error of α. These confidence intervals have the form:

One sided: $(\mu_{t_j} - \mu_c) \geq (\bar{X}_t - \bar{X}_c) - t_\alpha^{(1)}\sqrt{2}\, s/\sqrt{n}$ for $j=1,\ldots,m$.

Two sided: $(\mu_{t_j} - \mu_c) \in (\bar{X}_t - \bar{X}_c) \pm t_\alpha^{(2)}\sqrt{2}\, s/\sqrt{n}$ for $j=1,\ldots,m$.

Here $\bar{X}_c$ is the sample average of all control group observations, $\bar{X}_{t_j}$ is the sample average of all treatment group j observations $j=1,\ldots,m$ and s is the pooled estimate of the standard deviation.

Note that $t_\alpha^{(1)}$ and $t_\alpha^{(2)}$ are constants that depend on α. Dunnett's confidence intervals also have the nice property of symmetry: the type I error for each individual comparison is the same.

Sometimes it may be desired to simultaneously compare m new treatments

to $k \geq 2$ controls. In particular, it is often of interest to compare m new treatments to two controls. For example:

(A) - Two commonly used treatments (e.g., Aspirin and Tylenol) are each compared with m new treatments (e.g., m new pain relievers).

(B) - A standard treatment and a placebo are each compared with m new treatments. Two situations this might arise in are: (i) The standard treatment is expensive, has undesirable side effects or is otherwise impractical to use in some situations. The new treatments do not suffer from these problems and thus under certain conditions will be used if they can be shown to be better than placebo. (ii) The new treatments are in a developmental stage. Promising treatments (those which work better than no treatment) may be further developed and expanded testing will be done of treatments already performing better than the standard treatment.

Graham, et al. (1988) compared a particular class of antipyretic/analgesic treatment and a placebo to two standard therapies (considered controls here) in a study of undesirable side effects. They hypothesized that two standard treatments for cold symptoms (Aspirin and Ibuprofen) had adverse effects on the immune function (e.g., post virus challenge specific antibody response) and resulted in more virus shedding than did no treatment at all (placebo). They also hypothesized that a different class of cold symptom treatments, acetaminophen, had less adverse effects on the immune function and caused less virus shedding than did Aspirin or Ibuprofen.

As before, it is assumed that n observations are sampled from each treatment and control group with independence; those from the ith control group (c_i) distributed $N(\mu_{c_i}, \sigma^2)$ for $i=1,\ldots,k,$; and those from the jth

treatment group (t_j) distributed $N(\mu_{t_j}, \sigma^2)$ for j=1,...,m. Also $\bar{X}_{t_j}$ is the sample mean of all observations in the jth treatment group, while $\bar{X}_{c_i}$ is the sample mean of all observations in the ith control group.

It is now desired to give simultaneous confidence intervals for $(\mu_{t_j} - \mu_{c_i})$ where j=1,...,m and i=1,...,k. In Section II, Dunnett's methodology developed for k=1 controls is expanded on to work for k≥2 controls. The c onfidence intervals will be of the form:

$$\text{One sided: } (\mu_{t_j} - \mu_{c_i}) \geq (\bar{X}_{t_j} - \bar{X}_{c_i}) - d_\alpha^{(1)}\sqrt{2}\, s/\sqrt{n} \qquad (1)$$

$$\text{Two-sided: } (\mu_{t_j} - \mu_{c_i}) \in (\bar{X}_{t_j} - \bar{X}_{c_i}) \pm d_\alpha^{(2)}\sqrt{2}\, s/\sqrt{n} \qquad (2)$$

where $d_\alpha^{(1)}$ and $d_\alpha^{(2)}$ are the constants which make simultaneous coverage of the above one and two-sided confidence intervals equal to $1-\alpha$. These confidence intervals also have the property of symmetry.

II. DEVISING THE EXACT CONFIDENCE INTERVALS

The values for $d_\alpha^{(1)}$ and $d_\alpha^{(2)}$ making the overall type I error of the above one and two-sided confidence intervals equal to α are derived using order statistics of the standardized control means along with mutual independence of control means, treatment means and s. Two sided confidence interval results are more difficult to obtain and are dealt with first.

a. Two Sided Confidence Intervals

Define the standardized treatment group means and control groups means as:

$$T_j = (\mu_{t_j} - \bar{X}_{t_j})\sqrt{n}/\sigma \text{ for } j = 1...,m \qquad (3)$$

$$C_i = (\mu_{c_i} - \bar{X}_{c_i})\sqrt{n}/\sigma \text{ for } i = 1...,k. \qquad (4)$$

Now all two-sided confidence intervals given in (2) contain the true differences if and only if:

$$|T_j - C_i| < d_\alpha^{(2)}\sqrt{2} \cdot s/\sigma \text{ for all } i \text{ and } j. \tag{5}$$

If W and V are the maximum and minimum values among $C_1, C_2, \ldots, C_k$ then (5) is true if and only if:

$$T_j - W > - d_\alpha^{(2)}\sqrt{2} \cdot s/\sigma \text{ for all } j=1,\ldots,m \tag{6}$$

and

$$T_j - V < d_\alpha^{(2)}\sqrt{2} \cdot s/\sigma \text{ for all } j=1,\ldots,m. \tag{7}$$

Now $T_1, T_2, \ldots, T_m$ and $C_1, C_2, \ldots, C_k$ are all independent and identically distributed N(0,1) variables. The joint density of the order statistics (W, V) is easily obtained from a well known formula, e.g. in Mood, Graybill and Boes (1974) and is:

$$f(V=v, W=w) = 2\,\phi(v)\,\phi(w)\,[\Phi(w) - \Phi(v)]^{k-2}\, I(w>v)$$

where Φ and ϕ are the standard normal cumulative distribution and standard normal density function respectively. If $S_o = s/\sigma$ and r is the degrees of freedom of s, then $r(S_o)^2$ has a X^2_r distribution. Also (W, V) is independent of S_o and of $T_1, \ldots, T_m$. For any fixed values $S_o = s_o$, V=v and W=w, (w>v) the probability that $(\,|T_1 - C_i| < \sqrt{2}\, S_o\, d_\alpha^{(2)}\,)$ for all $i = 1,\ldots,k$ is the same as the probability that $(\,T_1 - v < \sqrt{2}\, s_o\, d_\alpha^{(2)}$ and $T_1 - w > \sqrt{2}\, s_o\, d_\alpha^{(2)}\,)$. This probability equals:

$$\text{Max}\,[0,\ (\Phi(v + \sqrt{2}\, s_o d_\alpha^{(2)}) - \Phi\,(w - \sqrt{2}\, s_o\, d_\alpha^{(2)})]. \tag{8}$$

By independence of the $T_j: j=1,\ldots,m$ and still conditioning on W=w, V=v and $S_0 = s_0$, the probability that $(\,T_j - v < \sqrt{2}\, s_o\, d_\alpha^{(2)}$ and $T_j - w > -\sqrt{2}\, s_o\, d_\alpha^{(2)}\,)$ for all j is:

$$[\text{Max}\,[0,\ (\Phi\,(v + \sqrt{2}\, s_o\, d_\alpha^{(2)}) - \Phi(w - \sqrt{2}\, s_o\, d_\alpha^{(2)}))]]^m.$$

Using the independence of (W, V) from S_o and integrating over their joint density gives the unconditional probability of coverage by the intervals in (2) as:

$$\int_{-\infty}^{\infty}\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \psi_r(rs_o^2)\ \phi(v)\ \phi(w)\ [\Phi(w)-\Phi(v)]^{k-2}$$

$$[\text{Max}\ [0,\ \Phi(v+\sqrt{2}\ \ d_\alpha^{(2)}s_o\ )-\Phi(w-\sqrt{2}\ d_\alpha^{(2)}s_o)]]^m\ d(rs_o^2)\ dv\ dw. \quad (9)$$

where $\psi_r(\cdot)$ is the standard X^2_r density function. This three dimensional interval can be evaluated using a powerful computer such as a Cray, FPS 264 or an IBM 3030.

When the probability in (9) equals $(1-\alpha)$, then the probability that all the intervals in (2) simultaneously contain the true differences is $(1-\alpha)$. This means that the overall Type I error is α. By iteration, from initial guesses, the value of $d_\alpha^{(2)}$ which will set the probability in (9) equal to $(1-\alpha)$ can be found.

Note that when k is two (i.e., there are two control groups) then $[\Phi(w)-\Phi(v)]^{k-2} = 1$, and so this term drops out of formula (9). When σ is known, or asymptotically when r is large, S_o can be set to 1 eliminating the inner integrand and reducing (9) to a two dimensional integral that can be easily evaluated on most mainframe computers. There do not appear to be any asymptotic simplifications of (9) as m and/or k get large.

b. <u>One Sided Confidence Limits</u>

The one sided lower confidence limits given in (1) will all contain the true values if and only if

$$(T_j-C_i) > \sqrt{2}\ S_o\ d_\alpha^{(1)} \text{ for all } j=1,\ldots,m \text{ and } i=1,\ldots,k. \quad (10)$$

which is true if and only if

$$(T_j-V) > \sqrt{2}\ S_o\ d_\alpha^{(1)} \text{ for all } j=1,\ldots,m. \quad (11)$$

With the same procedure used for 2 sided confidence intervals, the simultaneous coverage probability of the one sided upper limits given in (10) and (11) can be shown to equal the following integral:

$$\int_{-\infty}^{\infty}\int_{0}^{\infty} \psi_r(rs_o^2)\ \phi(v)\ [1-\Phi(v)]^{k-1}\ [\Phi(v+\sqrt{2}d_\alpha^{(1)}\ s_o)]^m\ d(rs_o^2)\ dv. \quad (12)$$

This two dimensional integral is easily evaluated on most mainframe computers. The value of $d_{\alpha}^{(1)}$ which makes the overall Type I error equal to $(1-\alpha)$ is obtainable through iteration from initial guesses.

When σ is known, or asymptotically when r is large, then S_o can be set to 1 eliminating the inner integrand and reducing (12) to a one dimensional integral. Note, that by symmetry, values for $d_{\alpha}^{(1)}$ used for one sided upper confidence limits will be the same as those needed for one sided lower confidence limits.

III. TABLED VALUES

Tables 1 and 2 give values of $d_{\alpha}^{(1)}$ and $d_{\alpha}^{(2)}$, respectively for $k=2$, $\alpha=.05$, $m=1,2,\ldots,10$, and various values of r. Values for $k \geq 3$ could be just as easily calculated but are not given here since it is felt that use of 3 or more controls will not be common.

The tables were constructed by numerical evaluation of the intergrals in (9) and (12) to an accuracy of 0.0001. The integration was performed with a Fortran program using an adaptive Romberg algorithm that was taken from Rabinowitz (1984), and altered to greatly reduce the number of computational steps. Secant iteration was used to obtain $d_{\alpha}^{(1)}$ and $d_{\alpha}^{(2)}$ to the nearest fourth decimal place. The results were then rounded to the highest third decimal place and included in the table. Good approximations of values of $d_{\alpha}^{(1)}$ (or $d_{\alpha}^{(2)}$) associated with r not in the tables are obtainable through standard linear interpolation of $d_{\alpha}^{(1)}$ (or $d_{\alpha}^{(2)}$) associated with tabled values of r.

The improvement from using the exact value for k=2 over using the best available upper bound (Tukey or Bonferroni) depends on α, r and m. Generally, the improvement increases with m and decreases with r. For instance, the exact value for $d_{\alpha}^{(1)}$ with (m=1, r=∞) is 1.917 which is 2.19% smaller than is the Bonferroni upper bound of 1.960. When (m=1, r=5) the exact value for $d_{\alpha}^{(1)}$ is 2.441, which is 5.06% smaller than is the Bonferroni upper bound of 2.571. When (m=5, r=∞) the exact value is 2.487, which is 3.45% smaller than is the Bonferroni upper bound of 2.576. Finally, when (m=5,r=5) the exact value of 3.469 is 13.96% smaller than is the Bonferroni upper bound of 4.032.

For small α, the improvement decreases as α decreases, due to the phenomenon of the Bonferroni approximation converging to the exact value as α decreases which was noted by Dunn (1958). Also, as k increases, the improvement of the exact value over upper bounds will increase for the same reason it does as m increases.

IV. ILLUSTRATIVE EXAMPLE

Below is an illustrative example of two treatments being simultaneously compared to a control and a placebo. It is adapted from one given by Villars (1951) and used in Dunnett (1955). The data represent measurements on the breaking strength of untreated fabric (placebo), fabric treated by an expensive standard method and fabric treated by two proposed less expensive methods.

Breaking Strength (lbs.)

	C_1-No Trt	C_2-Std Trt	T_1-New Trt 1	T_2-New Trt 2
	50	55	55	55
Observations	41	64	49	47
	41	61	52	48
Mean	45	61	52	50
Variance	21	27	9	14

Here m=2 and n=3. The Pooled variance estimate is $s^2 = 19$ and the degrees of freedom is 8. The estimated standard error of a difference between two means is $s\sqrt{2/n} = 3.56$. Symmetric two sided confidence intervals for $(\mu_{t_j} - \mu_{c_i})$ with an overall Type I error of α would take the form given by (2):

$$(\bar{X}_{t_j} - \bar{X}_{c_i}) \pm d_{\alpha}^{(2)}\sqrt{2/n}\, s \text{ for all i and j.}$$

Symmetric one sided lower confidence limits would be given by (1):

$$(\bar{X}_{t_j} - \bar{X}_{c_i}) - d_{\alpha}^{(1)}\sqrt{2/n}\, s \text{ for all i and j.}$$

The exact values for $d_{.05}^{(2)}$ and $d_{.05}^{(1)}$ obtained from Tables 2 and 1 along with commonly used upper bounds are given below.

	Exact	[Bonferroni	Upper Bounds Tukey	Scheffe]
$d_{.05}^{(2)}$	3.053	3.210	3.200	3.492
$d_{.05}^{(1)}$	2.588	2.751	N.A.	N.A.

Ninety-five per cent simultaneous confidence intervals for (treatment-control) differences derived from the exact and best upper bounds are now given.

Comparison	Confidence Intervals (95%)			
	Two Sided		One Sided (Lower)	
	Exact	Tukey	Exact	Bonferroni
$\mu_{t_1} - \mu_{c_1}$	(-3.87, 17.87)	(-4.39, 18.39)	> -2.22	> -2.96
$\mu_{t_1} - \mu_{c_2}$	(-19.87, 1.87)	(-20.39, 2.39)	> -18.22	> -18.96
$\mu_{t_2} - \mu_{c_1}$	(-5.87, 15.87)	(-6.39, 16.39)	> -4.22	> -4.96
$\mu_{t_2} - \mu_{c_2}$	(-21.87,-0.13)	(-22.39, 0.39)	> -20.22	> -20.96

The exact method finds the second new treatment to be significantly worse than the standard treatment when making two sided comparisons at α=.05. This statistical difference is not seen at α=.05 using the closest upper bound.

V. VARIATIONS ON ASSUMPTIONS

Formulas (9) and (12) can be altered to allow for unequal sample sizes and different variances within the control and treatment groups. One such variation would be having n_t observations sampled for each treatment group and n_c observations sampled for each control group with control and treatment variances the same. Under these assumptions, formula (9) becomes:

$$\int_{-\infty}^{\infty} \int_{-\infty}^{w} \int_{0}^{\infty} \psi_r(rs_o^2)\ 2\ \phi(v)\ \phi(w)\ [\Phi(w) - \Phi(v)]^{k-2}\ [\text{Max}\ [0,\ (\Phi(v + ((n_c+n_t)/n_t)^{1/2}\ d_\alpha^{(2)} s_o) - \Phi(w - ((n_c+n_t)/n_t)^{1/2}\ d_\alpha^{(2)} s_o))]^m\ d(rs_o^2)\ dv\ dw.$$

When given a total of n_o observations to be divided among m treatment groups and k control groups. It can be shown by calculus (as Dunnett (1955) did for k=1) that the optimal allocation of a fixed number of observations (n_o) to minimize the variance of $(\bar{X}_{t_j} - \bar{X}_{c_i})$ is: $n_t = \sqrt{k}\ n_o\ /\ ((\sqrt{k} + \sqrt{m})\ m)$ and $n_c = \sqrt{m}\ n_o\ /((\sqrt{k} + \sqrt{m})\ k)$.

VI. VARIATION ON THE CONFIDENCE INTERVALS

Comparing Both Control Groups to Each Other

In case (A) of the introduction, it may sometimes be of interest to also symmetrically compare the two control groups to each other, as well as, comparing each treatment to each control, with an overall Type I error of α. To do this requires building a two sided confidence interval for $(\mu_{c_1} - \mu_{c_2})$ of the form $(\bar{X}_{c_1} - \bar{X}_{c_2}) \pm d_\alpha \sqrt{2}s$ in addition to the one or two sided confidence intervals for the difference in (1). If the intervals for the differences in (1) are two sided, then the formula for simultaneous coverage is:

$$\int_{-\infty}^{\infty} \int_{0}^{\infty} \int_{e}^{w} \psi_r(rs_o^2)\ 2\ \phi(v)\ \phi(w)\ (\Phi(v + \sqrt{2}\ d_\alpha^{(2)} s_o) - \Phi(v - \sqrt{2}\ d_\alpha^{(2)} s_o))^m$$

$$dv\ d(rs_o^2)\ dw$$

where $e = w - d_\alpha^{(2)}\sqrt{2}\ s_o$. If the intervals for the differences in (1) are one sided, then the formula for simultaneous coverage is:

$$\int_{-\infty}^{\infty} \int_{0}^{\infty} \int_{e}^{w} \psi_r(rs_o^2)\ 2\ \phi(v)\ \phi(w)\ (\Phi(v + \sqrt{2}\ d_\alpha^{(1)} s_o)^m\ dv\ d(rs_o^2)\ dw$$

where $e = w - d_\alpha^{(1)}\sqrt{2}\ s_o$.

Other Variations

It may be desired to have two sided confidence intervals for the differences between all treatments and the first control and one sided confidence limits for the differences between all treatments and the second control. Sometimes the mean effect of the first control may be known while that of the second control is not. Both of these previous situations may occur when the second control is a placebo. For each of these situations it is possible to produce symmetric confidence intervals having an overall Type I error of α using modifications of the previous methodology. The formulas needed, however, are quite complicated.

VII. ACKNOWLEDGEMENTS

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TABLE 1: Exact Values of $d^{(1)}_{.05}$ for k = 2 Controls, m New Treatment and r Degrees of Freedom.

r \ m	1	2	3	4	5	6	7	8	9	10
5	2.441	2.896	3.154	3.333	3.469	3.579	3.670	3.748	3.816	3.876
6	2.337	2.752	2.986	3.148	3.271	3.370	3.452	3.523	3.584	3.638
7	2.268	2.656	2.874	3.025	3.139	3.231	3.307	3.372	3 429	3.480
8	2.218	2.588	2.795	2.937	3.045	3.132	3.204	3.265	3.319	3.367
9	2.180	2.536	2.735	2.871	2.974	3.057	3.126	3.185	3.237	3.282
10	2.151	2.496	2.688	2.820	2.920	3.000	3.066	3.123	3.172	3.216
11	2.128	2.464	2.651	2.779	2.876	2.954	3.018	3.073	3.121	3.164
12	2.109	2.438	2.621	2.746	2.840	2.916	2.979	3.033	3.080	3.121
13	2.093	2.417	2.596	2.718	2.811	2.885	2.946	2.999	3.045	3.085
14	2.079	2.393	2.574	2.695	2.786	2.858	2.919	2.970	3.015	3.055
15	2.067	2.382	2.556	2.675	2.764	2.836	2.895	2.946	2.990	3.029
16	2.057	2.369	2.540	2.657	2.745	2.816	2.875	2.925	2.968	3.007
17	2.044	2.357	2.526	2.642	2.729	2.799	2.857	2.906	2.949	2.987
18	2.041	2.346	2.514	2.657	2.715	2.784	2.841	2.840	2.932	2.970
19	2.034	2.337	2.503	2.642	2.702	2.770	2.827	2.876	2.918	2.955
20	2.028	2.239	2.494	2.606	2.691	2.758	2.815	2.863	2.904	2.941
24	2.008	2.303	2.463	2.573	2.655	2.721	2.775	2.822	2.863	2.898
30	1.990	2.277	2.433	2.540	2.620	2.684	2.737	2.782	2.822	2.856
40	1.971	2.252	2.404	2.508	2.856	2.648	2.699	2.743	781	2.815
60	1.953	2.227	2.376	2.477	2.552	2.613	2.663	2.705	2.742	2.775
120	1.935	2.203	2.348	2.446	2.519	2.578	2.626	2.668	2.703	2.735
∞	1.917	2.179	2.320	2.415	2.487	2.544	2.591	2.631	2.665	2.696

TABLE 2: Exact Values of $d^{(2)}_{.05}$ for k = 2 Controls, m New Treatments and 4 Degrees of Freedom.

r \ m	1	2	3	4	5	6	7	8	9	10
5	3.031	3.529	3.815	4.012	4.164	4.285	4.387	4.475	4.550	4.618
6	2.863	3.305	3.557	3.732	3.866	3.972	4.062	4.139	4.206	4.265
7	2.752	3.157	3.388	3.547	3.670	3.767	3.849	3.920	3.980	4.034
8	2.673	3.053	3.268	3.417	3.531	3.622	3.698	3.764	3.821	3.871
9	2.614	2.975	3.180	3.321	3.429	3.515	3.587	3.649	3.703	3.751
10	2.569	2.916	3.112	3.247	3.350	3.432	3.501	3.561	3.612	3.657
11	2.532	2.868	3.057	3.188	3.287	3.366	3.433	3.490	3.539	3.584
12	2.503	2.829	3.013	3.140	3.236	3.313	3.378	3.433	3.481	3.523
13	2.478	2.797	2.977	3.100	3.194	3.269	3.331	3.386	3.432	3.474
14	2.457	2.770	2.946	3.066	3.158	3.232	3.293	3.346	3.391	3.432
15	2.440	2.747	2.919	3.038	3.128	3.200	3.260	3.312	3.356	3.396
16	2.424	2.727	2.897	3.013	3.102	3.172	3.231	3.282	3.326	3.365
17	2.411	2.710	2.877	2.992	3.079	3.148	3.206	3.256	3.300	3.338
18	2.397	2.694	2.859	2.973	3.059	3.127	3.185	3.234	3.276	3.314
19	2.389	2.681	2.844	2.956	3.041	3.108	3.165	3.214	3.256	3.293
20	2.379	2.669	2.830	2.941	3.025	3.092	3.148	3.196	3.237	3.274
24	2.350	2.631	2.787	2.894	2.975	3.040	3.094	3.140	3.180	3.216
30	2.321	2.594	2.745	2.848	2.926	2.989	3.041	3.085	3.124	3.158
40	2.293	2.558	2.704	2.804	2.879	2.939	2.989	3.032	3.069	3.103
60	2.266	2.522	2.664	2.760	2.833	2.891	2.939	2.980	3.016	3.048
120	2.239	2.488	2.624	2.717	2.788	2.843	2.890	2.930	2.964	2.995
∞	2.213	2.456	2.586	2.676	2.743	2.797	2.842	2.880	2.913	2.942

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20. ABSTRACT

Dunnett (1955) developed a procedure comparing m treatments to one control with an exact overall type I error of α when all sampling distributions are normal. Sometimes it is desirable to compare m treatments to $k \geq 2$ controls. In particular, it is often desired to compare m treatments with two controls. For instance, several new treatments (e.g., pain relievers) could be compared to two standard treatments (e.g., Aspirin and Tylenol). Alternatively, a standard treatment could be very expensive, difficult to apply and/or have bad side effects, making it useful to compare each new treatment to both standard treatment and no treatment (Placebo).

Dunnett's method is expanded here to give comparisons of mean values for m treatments to mean values for $k \geq 2$ controls at an exact overall type I error of α when all sampling distributions are normal. Tabled values needed to make exact simultaneous comparisons at $\alpha=.05$ are given for $k=2$. An application is made to an illustrative example from the literature.